AMENDMENTS TO THE SPECIFICATION

1/ Please amend the paragraph following the title "Related Applications" on page 1 of the application as follows:

The present application is a U.S. National Phase Application under 35 U.S.C § 371 of International Application PCT/US2003/17410 (published PCT application No. WO 03/101474) filed June 2, 2003, which ~~This application~~ claims the benefit of U.S. Provisional Application 60/406,033 (filed Aug. 27, 2002) and U.S. Provisional Application 60/384,171 (filed May 31, 2002). Each of the above-cited patent applications is incorporated herein by reference in its entirety. ~~both of which are hereby incorporated by reference in their entirety.~~

2/ Please amend the paragraph starting at the end of page 24 and ending at the beginning of page 25 of the application, as originally filed, as follows:

Examples of pharmaceutical formulations of the above chemotherapeutic agents include, but are not limited to, BCNU (i.e., carmustine, 1,3-bis(2-chloroethyl)-1-nitrosurea, BiCNU™), cisplatin (cis-platinum, cis-diamminedichloroplatinum, ~~Platinol™~~ PLATINOL™), doxorubicin (hydroxyl daunorubicin, ~~Adriamycin™~~ ADRIAMYCIN™), gemcytabine (difluorodeoxycytidine, ~~Gemzar™~~ GEMZAR™), hyrdoxyurea (hyroxycarbamide, Hydrea™ HYDREA™), paclitaxel (~~Taxol™~~ TAXOL™), temozomide (TMZ, ~~Temodar™~~ TEMODAR™), topotecan (~~Hycamtin™~~ HYCAMTIN™), fluorouracil (5-fluorouracil, 5-FU, ~~Adrucil™~~ ADRUCIL™), vincristine (VCR, ~~Oncovin™~~ ONCOVIN™) and vinblastine (~~Velbe™~~ VELBE™ or ~~Velban™~~ VELBAN™).

3/ Please amend the first paragraph on page 7 of the application, as originally filed, as follows:

Figure 1 depicts the effect of TEMODAR™ ~~temodar~~ in combination with chlorotoxin in vitro. D54 glioma cells were incubated with saline alone (control), TEMODAR™ ~~temodar~~ alone, TEMODAR™ ~~temodar~~ plus chlorotoxin, or pretreated with chlorotoxin twenty-four hours prior to TEMODAR™ ~~temodar~~ treatment.

4/ Please amend the second paragraph on page 7 of the application, as originally filed, as follows:

Figure 2 depicts the effect of chlorotoxin on TEMODAR™ ~~temodar~~ efficacy in vivo. Nude mice with established U251 glioma flank tumors were treated with saline alone (control), TEMODAR™ ~~temodar~~ alone, or TEMODAR™ ~~temodar~~ plus chlorotoxin.

5/ Please amend Table 3 at the end of page 30 and beginning of page 31 of the application, as originally filed, as follows:

TABLE 3. IC_{50} of Chemotherapeutic Agents in Multiple Cell Lines

Cell Line	Drug	IC_{50}
D54-MG	Doxorubicin	60.0 ng/ml
D54-MG	Paclitaxel	10.5 nM
D54-MG	TEMODAR™ ~~Temodar~~	0.12 mM
D54-MG	Cisplatin	0.010 mg/ml
D54-MG	5-Fluorouracil	0.0015 mg/ml
U251	Doxorubicin	30.0 ng/ml
U251	Paclitaxel	8.0 nM
U251	Temodar	0.15 mM
SKMEL28	Doxorubicin	40.0 ng/ml
SKMEL28	TEMODAR™ ~~Temodar~~	0.03 mM
SKMEL28	Cisplatin	0.008 mg/ml
SKMEL31	Doxorubicin	35.0 ng/ml
SKMEL31	Paclitaxel	25 nM
SKMEL31	Temodar	0.15 mM
PC-3	Hydroxyurea	35 mM

6/ Please amend the second paragraph of Example 2 on page 31 of the application, as originally filed, as follows:

The effect of adding chlorotoxin in combination with TEMODAR™ ~~Temodar~~ on D54-MG cell proliferation is shown in FIG. 1. The level of TEMODAR™ ~~Temodar~~ used in this experiment (0.050 mM) is about thirty-fold lower than the concentration necessary to kill these cells and produce a lower optical density value (see Table 2). Chlorotoxin (TM-601) alone had

no effect on cell growth. Chlorotoxin when added at the same time as TEMODAR™ ~~Temodar~~ did not produce any effect but when chlorotoxin was added twenty-four hours prior to TEMODAR™ ~~Temodar~~, a concentration of 0.050 mM TEMODAR™ ~~Temodar~~ reduced cell proliferation equivalent to a level usually observed with a thirty-fold higher concentration of TEMODAR™ ~~Temodar~~. These results demonstrate that administration of chlorotoxin, prior to administration of TEMODAR™ ~~Temodar~~, sensitized cancer cells to the effects of TEMODAR™ ~~Temodar~~.

7/ Please amend the paragraph starting on page 31 and ending on page 32 of the application, as originally filed, as follows:

The purpose of this study was to determine whether hydroxyurea or TEMODAR™ ~~temodar~~ combined with chlorotoxin were sufficient to inhibit tumor growth as indicated from in vitro studies with glioma cell lines. Other studies indicated that chlorotoxin, pre-incubated with human cancer cell lines, greatly sensitized the cells to TEMODAR™ ~~temodar~~, a chemotherapeutic, tumor cell killing agent. Combination treatment with chlorotoxin with hydroxyurea or TEMODAR™ ~~temodar~~ in mice with glioma flank tumors was compared to the treatment group of hydroxyurea or TEMODAR™ ~~temodar~~ alone and saline alone. Hydroxyurea and TEMODAR™ ~~temodar~~ dosage was based on the lowest dosage (10 mg/kg body weight) used in previous studies to determine clearance from the body in the treatment of sickle cell disease paradigm in nude mice (Iyamu et al. (2001) Chemotherapy 47, 270-278).

8/ Please amend the third paragraph on page 32 of the application, as originally filed, as follows:

Mice with established flank tumors were each treated with 0.100 ml injection (i.p) of sterilized solutions consisting of either of saline, saline and hydroxyurea or TEMODAR™ ~~temodar~~ (13.2 mg/kg body weight), or saline, hydroxyurea or TEMODAR™ ~~temodar~~ (13.2 mg/kg) and chlorotoxin (0.080 mg/kg body weight). Tumor volume was calculated based on the measurements with the same set of calipers on the indicated days by determining the length x times x width x times x height of the tumor of non-anesthetized mice. As each animal had different-sized tumors at the beginning of the experiment, the data is presented in final form as percent change of the tumor growth from the initial date of the injection protocol. Statistical

significance was determined according to a one-way ANOVA test. At a level where TEMODAR™ ~~temodar~~ alone has little effect on the growth of the xenografted tumor, TEMODAR™ ~~temodar~~ combined with chlorotoxin dramatically decreased the growth of the tumor (FIG. 2).